Application No.: 09/688,017

Page 2

In response to the Notice to Comply, Applicants submit herewith the required paper copy and computer readable copy of the Sequence Listing. Please amend the specification in adherence with 37 C.F.R. §§ 1.821-1.825 as follows.

### In the Specification:

Y

Please replace the paragraph beginning at page 1, line 22, with the following:

--PDZ domains of proteins are named after three prototypical proteins:
PSD95, Drosophila large disc protein and Zonula Occludin 1 protein (Gomperts et al., 1996, Cell 84:659-662). PDZ domain-containing proteins are involved in synapse formation by organizing transmembrane neurotransmitter receptors through intracellular interactions. PDZ domains contain the signature sequence GLGF (SEQ ID NO:29). In the nervous system, typical PDZ domain-containing proteins contain three PDZ domains, one SH3 domain and one guanylate kinase domain. Examples of intracellular PDZ domain-containing proteins include LIN-2, LIN-7 and LIN-10 at the pre-synapse, and PSD95 at the post-synapse.--

Please replace the paragraph beginning at page 12, line 1, with the following:

--5.3 As used herein, the term "PDZ domain" refers to protein sequence (i.e., modular protein domain) of approximately 90 amino acids, characterized by homology to the brain synaptic protein PSD-95, the Drosophila septate junction protein Discs-Large (DLG), and the epithelial tight junction protein ZO1 (ZO1). PDZ domains are also known as Discs-Large homology repeats ("DHRs") and GLGF (SEQ ID NO:29) repeats). PDZ domains generally appear to maintain a core consensus sequence (Doyle, D. A., 1996, Cell 85: 1067-1076).--

Please replace the paragraph (TABLE 2) beginning at page 26, line 1, with the following (see attached sheets).

Al

A2

# PDZ-LIGAND/PDZ INTERACTION SUMMARY

### TABLE 2

. ,			SEQ			1	Γ		· · · ·		I			ı — —	1	
PDZ LIGAND	CODE	SEQ	ID NO:	CASK	MPP1	DLG1	PSD95	NeDLG	TAX33	SYN1a	TAX 43	LDP	LIM	LIMK1	LIMK2	MPP:
CD6	AA6L	ISAA	14													
CD49E (alpha-4)	AA11L	TSDA	24													
CD49F (Aform, alpha6)	AA12L	TSDA	24													
CD166 (CD6L)	AA20L	KTEA	64			<u> </u>										
CD148	AA55L	KTIA	278													l
CC CKR-2	AA42L	KEGA	283									-				-
CD138 (syndecan)	AA18L	EFYA	89	*												
CD148 (DEP-1)	AA19L	GYIA	119													
CD98 (2F4)	AA15L	PYAA	54													G
CLASP-1	AA1L	SAEV	284			G	Α	G							<del></del>	
CLASP-4	AA3L-V	YAEV	228			Α	Α	Α				Α				
NMDA	AA34.2L	ESDV	263		Α	A/G	A/G	A/G		G	Α			Α		G
VCAM1	AA17L	KSKV	163		A	Α		Α				Α				
CLASP-2	AA2L	ssvv	223			A/G	A/G	A/G								
CD95 (Apo-1/Fas)	AA13L	QSLV	44			A/G	A/G	A/G								
KV1.3	AA33L	FTDV	238			A/G*	A/G*	A/G						Α		
DNAM-1	AA22L	KTRV	74		Α	Α	A/G	Α					Α			G
CD83	AA47L	TELV	248			А	Α	Α								
CD44 (long form)	AA9L	KIGV	104		G											
Neurexin	AA38L	EYYV	268	G*	A*	A/G	A/G	G		Α	Α			А		
CD97 (CD55L)	AA14L	ESGI	49			Α										
Glycophorin C	AA37L	EYFI	273		*	G	G	G								Α
CDW128A (IL8RA)	AA29.1L	SSNL	69			Α		Α								
CD3n	AA4 L	SSQL	4			Α	Α									
LPAP	AA30L	VTAL	84			Α										
CD46 (form 1)	AA10L	FTSL	109			A/G	A/G	G								
CDW128B (IL8RB)	AA29.2L	STTL	233			A/G	Α	A/G								
DOCK2	AA40L	STDL	243			Α	A/G	G		G						
CD34	AA7L	DTEL	149			Α	Α	G								
CD5	AA49L	AQRL	285													
CC CKR-4	AA44L	HDAL	286													
FceRlb	AA25L	PIDL	129													
FasLigand	AA23L-M	LYKL	79													
CD62E	AA48L	SYIL	168													
CC CKR-1R	AA41L	SAGF	287													
CDW125 (IL5R)	AA28L	DSVF	94													
BLR-1	AA45L	LTTF	253													
CC CKR-3	AA43L	SIVF	288													
				CASK	MPP1	DLG1	PSD95	NeDLG	TX33	SYN1a	TX 43	LDP	LIM	LIMK	LIMK2	MPP

<sup>\*</sup> Interactions described in the scientific literature

## A3

# PDZ-LIGAND/PDZ INTERACTION SUMMARY

## TABLE 2 CONTINUED

NOS1	AF6	PTN-4	prIL16	3	K559	RGS12	K316	DVL1	TAX 40	TIAM1	MINT1	K303	CBP	MINT3	TAX 2	K561	PDZ LIGAND
	<u> </u>			Α		<u> </u>						ļ	ļ	ļ			CD6
				A/G	ļ	ļ		ļ		<u> </u>		<u> </u>	<del> </del>				CD49E (alpha-4)
				A/G							——		ļ	1			CD49F (Aform, alpha6)
		ļ									ļ		ļ				CD166 (CD6L)
							ļ						ļ				CD148
	<u> </u>	ļ									<u> </u>						CC CKR-2
				A/G						Α			<u> </u>	ļ			CD138 (syndecan)
													<u> </u>		_		CD148 (DEP-1)
													ļ			l	CD98 (2F4)
																	CLASP-1
	Α			Α							Α_						CLASP-4
		A/G		A/G	<u> </u>	A/G	L	Α			A/G				Α	G	NMDA
				Α						Α		Α					VCAM1
				Α													CLASP-2
				A/G													CD95 (Apo-1/Fas)
				Α		Α		Α			G						KV1.3
	Α			Α		Α											DNAM-1
																	CD83
			G								G						CD44 (long form)
	Α		Α	Α		Α		Α	Α	Α	A/G						Neurexin
				Α													CD97 (CD55L)
	Α			Α							Α						Glycophorin C
																	CDW128A (IL8RA)
				A/G							A/G						CD3n
											G						LPAP
																	CD46 (form 1)
				Α		*											CDW128B (IL8RB)
				,,												G	DOCK2
							-						l				CD34
																	CD5
																	CC CKR-4
											Α		<del> </del>				FceRib
		ļ											<del>                                     </del>			G	
										-						G	FasLigand CD62E
		-										<del></del>	-				CC CKR-1R
		_															
		G				G						ļ	<del> </del>		-		CDW125 (IL5R)
						-			-		G		-				BLR-1
							<u></u>					ļ	<del> </del>	<u>                                     </u>	<del></del>		CC CKR-3
1051	AF6	PTN-4	prIL16	41.8	K559	RSG12	K316	DVL1	TX 40	TIAM1	MINT1	K303	CBP	мімтз	TX 2	K561	

<sup>\*</sup> Interactions described in the scientific literature

Application No.: 09/688,017

Page 3

A4

Please replace the paragraph (TABLE 3) beginning at page 33, line 1, with the following (see attached sheets).

Please replace the paragraph beginning at page 50, line 25, with the following:

--As noted *supra*, PCR primers were designed to include endonuclease restriction sites to facilitate ligation of PCR fragments into a GST gene fusion vector (pGEX-3X; Pharmacia, GenBank accession no. XXU13852) in-frame with the glutathione-S transferase coding sequence. This vector contains a IPTG inducible lacZ promoter. The pGEX-3X vector was linearized using Bam HI and Eco RI or, in some cases, Eco RI or Sma I, as shown in TABLE 3, and dephosphorylated. For most cloning approaches, double digest with Bam HI and Eco RI was performed, so that the ends of the PCR fragments to clone were Bam HI and Eco RI. In some cases, restriction endonuclease combinations used were Bgl II and Eco RI, Bam HI and Mfe I, or Eco RI only, Sma I only, or BamHI only (see TABLE 3). When more than one PDZ domain was cloned, the DNA portion cloned represents the PDZ domains and the cDNA portion located between individual domains. Precise locations of cloned fragments used in the assays are indicated in TABLE 3. DNA linker sequences between the GST portion and the PDZ domain containing DNA portion vary slightly, dependent on which of the above described cloning sites and approaches were used. As a consequence, the amino acid sequence of the GST-PDZ fusion protein varies in the linker region between GST and PDZ domain. Protein linkers sequences corresponding to different cloning sites/approaches are shown below. Linker sequences (vector DNA encoded) are bold, PDZ domain containing gene derived sequences are in italics.

- 1) **GST—BamHI**/BamHI— PDZ domain insert **Gly--Ile**—PDZ domain insert
- 2) **GST—BamHI**/BglII—PDZ domain insert **Gly—Ile**—PDZ domain insert
- 3) GST—EcoRI/EcoI—PDZ domain insert Gly—Ile—Pro—Gly--Asn—PDZ domain insert (SEQ ID NO:258)
- 4) GST--Smal/Smal—PDZ domain insert Gly—Ile—Pro—PDZ domain insert--

A5

TABLE 3 PDZ DOMAINS

Key:

_	PROTELIN	ACC:#	AMINO ACID SEQUENCE*	CLON.	FORWARD	REVERSE
H				SILES	PRIMER	PRIMER
CASK	CASK	Y17138	AA495-584;	Bam HI /	6CAF	7CAR
			PDZ domain 1 (of 1)	Eco RI		
					5, -	5'-
					TCGGATCCAT	TCGGAATTCAG
			HVIRVRLVQFQKNTDEPMGITLK		GTGACCAGAG	ACTGAGTGCGG
			MNELNHCIVARIMHGGMIHRQGT		TTCGG-3'	TA-3'
			LHVGDEIREINGISVANQTVEQL		(SEQ ID	(SEQ ID
			QKMLREMRGSITFKIVPSYRTQS		NO:322)	NO:323)
			LNSS (SEQ ID NO:292)			
			•		N1471-1494 N1761-1738	N1761-1738

ř ř	F D
63MPR 5'- ACGGATCCGCT GGTTGGGAATT ACTT-3' (SEQ ID NO:325) N568-543	5'- CGGAATTCGGT GCATAGCCATC -3' (SEQ ID NO:327) N1442-1421
62MPF  5'- GGGATCCGGA  AAGTGCGACT CATAC-3' (SEQ ID NO:324)  NO:324)	1DF 5'- TCGGATCCAG GTTAATGGCT CAGATG-3' (SEQ ID NO:326) N815-841
Bam HI Bam HI	Bam HI / Eco RI
AA101-186; PDZ domain 1 (of 1) RKVRLIQFEKVTEEPMGITLKLN EKQSCTVARILHGGMIHRQGSLH VGDEILEINGTNVTNHSVDQLQK AMKETKGMISLKVIPNQREFIVT D (SEQ ID NO:293)	AA275-477; PDZ domains 1-2 (of 3) QVNGTDADYEYEEITLERGNSGL GFSIAGGTDNPHIGDDSSIFITK IITGGAAAQDGRLRVNDCILQVN EVDVRDVTHSKAVEALKEAGSIV RLYVKRRKPVSEKIMEIKLIKGP KGLGFSIAGGVGNQHIPGDNSIY VTKIIEGGAAHKDGKLQIGDKLL
M64925	U13897
55 Kd erythrocyte membrane protein	human homolog of Drosophila discs large protein
MPP1	DLG1

DFVYLKVAKPTSMYMNDGYA*PNS* S (SEQ ID NO:294)

11PSR		5,-	TCGGAATTCGC	TATACTCTTCT	GG-3,	(SEQ ID	NO:329)		N2191-2168										
8PSF		5′-	TCGGATCCTT	GAGGGGGAGA	TGGA-3'	(SEQ ID	NO:328)		N1150-1173								•		
Bam HI /	Eco RI																		
AA387-724;		PDZ domains 1-3 (of 3)		LEGEGEMEYEEITLERGNSGLGF	SIAGGIDNPHIGDDPSIFITKII	PGGAAAQDGRLRVNDSILFVNEV	DVREVTHSAAVEALKEAGSIVRL	YVMRRKPPAEKVMEIKLIKGPKG	LGFSIAGGVGNQHIPGDNSIYVT	KIIEGGAAHKDGRLQIGDKILAV	NSVGLEDVMHEDAVAALKNTYDV	VYLKVAKPSNAYLSDSYAPPDIT	TSYSQHLDNEISHSSYLGTDYPT	AMTPTSPRRYSPVAKDLLGEEDI	PREPRRIVIHRGSTGLGFNIVGG	EDGEGIFISFILAGGPADLSGEL	RKGDQILSVNGVDLRNASHEQAA	IALKNAGQTVTIIAQYKPE <i>FIV</i>	(SEQ ID NO:295)
U83192																			
human post-	synaptic	density	protein 95																
PSD95																			

Ö

72NEDR	i.	-	CAA TTGAATTCGAG	AAAA   GCTGCCTGGCT	TG- TGGC-3'	(SEQ ID	NO:331)		N1186-1161	ر <del>ن</del>		93TAR		- 2, -	cca   cargaattcca	CCT GAACTTTGGG	3-3'   TGTATCGC-3'	(SEQ ID	NO:333)	34   N497-468
71NEDF	ì	٦, '-	CAGGATCCAA	TATGAGGAAA	TCGTACTTG-	3,	(SEQ ID	NO:330)		N608-635		92TAF		2, -	GTGGGATCCA	CTCCCACCCT	CGAGTAG-3'	(SEQ ID	NO:332)	N208-234
Bam HI /	Eco RI											Bam HI /	Eco RI							
AA205-1171;	PDZ domains 1-2 (of 3)		QYEEIVLERGNSGLGFSIAGGID	NPHVPDDPGIFITKIIPGGAAAM	DGRLGVNDCVLRVNEVEVSEVVH	SRAVEALKEAGPVVRLVVRRRQP	PPETIMEVNLLKGPKGLGFSIAG	GIGNQHIPGDNSIYITKIIEGGA	AQKDGRLQIGDRLLAVNNTNLQD	VRHEEAVASLKNTSDMVYLKVAK	PGSPR (SEQ ID NO:296)	AA73-162;	PDZ domain 1 (of 1)		HSHPRVVELPKTDEGLGFNVMGG	KEQNSPIYISRIIPGGVAERHGG	LKRGDQLLSVNGVSVEGEHHEKA	VELLKAAKDSVKLVVRYTPKVLE	FIVTN (SEQ ID NO:297)	
U49089												AF028826								
presynaptic	protein	saoloz	(neuroendo-	crine-dlg)								tax	interaction	protein 33						
NeDLG												TAX33								

Af

o

125SYR	2,-	GTAGAATTCTT	GAAATACGGTG	AGAC-3'	(SEQ ID	NO:335)	NE 2 C C C C	TCC-0/CN
124SYF	5′-	TACGGATCCA	900900909	CGTGAC-3'	(SEQ ID	NO:334)	100 0001	TO C - 6 / 7NT
Bam HI / 124SYF Eco RI								
AA96-189 PDZ domain 1 (of 1)		QRRRVTVRKADAGGLGISIKGGR	ENKMPILISKIFKGLAADQTEAL	FVGDAILSVNGEDLSSATHDEAV	QVLKKTGKEVVLEVKYMKDVSPY	FKNSS (SEQ ID NO:298)		
U40571								
SYN 1 α alpha1- syntrophin								
SYN 1 α								

98TAR		5′-	CGGAATTCAAC	GCCTGCACCGC	CTC-3,	(SEQ ID	NO:337)		N267-231
97TAF		2, -	TCTGGATCCA	GAAGCGTGGC	GTGAAGG-3'	(SEQ ID	NO:336)		N37-63
Bam HI / 97TAF	Eco RI					<u>.</u>			
AA15-85	PDZ domain 1 (of 1)			QKRGVKVLKQELGGLGISIKGGK	ENKMPILISKIFKGLAADQTQAL	YVGDAILSVNGADLRDATHDEAV	QALQFIVTN (SEQ ID	NO:299)	
AF028828 AA15-85									
TAX43 human tax	interaction	protein 43							
TAX43									

147LIR 5'- CATGAATTCGC TAGAGCCGCCT TGCTT-3' (SEQ ID NO:339)	NZ / 6 - Z 3 9	183LR	2′ -	CTTGAATTCAG	CAGATGCTCTT	TGCAGAGTC-	3,	(SEQ ID	NO:341)	N350-320	53LIRP		5′-	TCGCCCGGGTC	ATGCTCGAGGG	TC-3,	(SEQ ID	NO:343)	N874-851
146LIF 5'- CCAGGATCCG CGGAATGACC ACCCAGC-3' (SEQ ID NO:338)	N129-135	182LF	5′-	TTAGGATCCT	GAGCAAGTAC	AGTGTGTCAC	-3,	(SEQ ID	NO:340)	N86-115	52LIFP		- 2	CTGCCCGGGA	CCGTCACCCT	GGTGTCC-3'	(SEQ ID	NO:342)	N570-597
Bam HI / Eco RI			20 20 31 31								SMA I				•	a			
AA46-88 PDZ domain 1 (of 1) RGMTTQQIDLQGPGPWGFRLVGR KDFEQPLAISRVTPGSKAALASS (SEQ ID NO:300)		AA29-112;		LSNYSVSLVGPAPWGFRLQGGKD	FNMPLTISSLKDGGKAAQANVRI	GDVVLSIDGINAQGMTHLEAQNK	IKGCTGSLNMTLQRASC (SEQ	ID NO:301)			AA194-291;	PDZ domain 1 (of 1)		TVTLVSIPASSHGKRGLSVSIDP	PHGPPGCGTEHSHTVRVQGVDPG	CMSPDVKNSIHVGDRILEINGTP	IRNVPLDEIDLLIQETSRLLQLT	LEHD <i>PGIHRD</i> (SEQ ID	NO:302)
U90878		AF061258									NM	002314							
lim domain protein clp-36		Human LIM	J. Oceili								human LIM	domain	kinase 1						
LDP		LIM									LIMK1								

A4

5'- 5'-	GTTCAATCAAC AGCTGAAG-3' (SEQ ID NO:345)		MR		ATGGAATTCCT	GGTAGTTGGGC	AGGATC-3'	(SEQ ID	NO:347)		N828-801	
ر ر آ ا	IIAU .	N545-573	142MF 143MR	ر بر	GGATCCA	GCCTGTACCT GGI	CCCGATGC- AGG	ES)	(SEQ ID NO:	NO:346)	N82	N542-569
ECO RI 5'-	ACC 3, 3, (SI	N5	Bam HI / 142	Eco RI	TC	)   	<u> </u>	3,	(S)	ON		N54
AA185-275; PDZ domain 1 (of 1) PYSVTI.ISMPATTEGRRGFSVSV	ESACSNYATTVQVKEVNRMHISP NNRNAIHPGDRILEINGTPVRTL RVEEVEDAISQTSQTLQLLIEHE FIVTN (SEQ ID NO:303)		AA185-273;	PDZ domain 1 (of 1)	QPVPPDAVRMVGIRKTAGEHLGV	TFRVEGGELVIARILHGGMVAQQ	GLLHVGDIIKEVNGQPVGSDPRA	LQELLRNASGSVILKILPNYQVF	IVTD (SEQ ID NO:304)			
D45906			X82895									
LIMK2 human LIM domain kinase 2			maguk p55	subfamily member 2	(DLG2)							
LIMK2			MPP2									

AH
----

NOS1	human	U17327	AA239-988;	Bam HI /	/ 155NOF	156NOR
	neuronal		PDZ domain 1 (of 1)	Eco RI		
	nitric	,			5'-	5′-
	oxide		IQPNVISVRLFKRKVGGLGFLVK		AGCGGATCCA	GAAGAATTCAG
	synthase		ERVSKPPVIISDLIRGGAAEQSG		GCCCAATGTC	GGCCCCTCAGA
			LIQAGDIILAVNGRPLVDLSYDS		ATTTC-3'	ATG-3'
			ALEVLRGIASETHVVLILRGP <i>EF</i>		(SEQ ID	(SEQ ID
			IVTD (SEQ ID NO:305)		NO:348)	NO:349)
					N711-733	N994-970

67AFR		5,-	TAGAATTCACC	CTGCTTTGCTA	CTTC-3'	(SEQ ID	NO:351)	N3239-3214	
66AFF		- 2	TCGGATCCTG	AGGAAAGAAC	CTGAA-3'	(SEQ ID	NO:350)	N2946-2970   N3239-3214	
/ IH we	Eco RI								
AA985-1077;	PDZ domain 1 (of 1)		LRKEPEIITVTLKKQNGMGLSIV	AAKGAGQDKLGIYVKSVVKGGAA	DVDGRLAAGDQLLSVDGRSLVGL	SQERAAELMTRTSSVVTLEVAKQ	GEFIVTD (SEQ ID NO:306)		
U02478									
af-6	protein								
AF6									

•	1
A	L
π	1

248PTR	1	ATCGAATTCAG	CATTAGGICGA ACTAG-3'	(SEQ ID	NO:353)	N2595-2569	76PRR	_	ı	GTGAATTCCTT	GGACTGGAGGC	TTTTC-3'	(SEQ ID	NO:355)		N1157-1129					
	- 2, -		AATCAGAATG   CA AAACCTG-3'   AC	(SEQ ID (S		N2312-2338 N2		<del>-</del>	- /2	ACGGGATCCA GT	TGTCACCATC   GG	TTACAC-3' TT	(SEQ ID (S			N503-528 N1	<del></del>		•		
. / 247PTF	- ,2	ATCC	AATC	) (SEC	NO:352)	N231	: / 75PRF		5′-	ACGC	TGT	TTAC	) (SE(	NO:354)		N503					
Bam HI Eco RI	-					•	Bam HI	Eco RI													
AA774-862; PDZ domain 1 (of 1)		LIRMKPDENGRFGFNVKGGYDQK	MPVIVSKVAPGIPADLCVPKLNE GDQVVLINGRDIAEHTHDQVVLF	IKASCERHSGELMLLVRPNA <i>EFI</i>	VTD (SEQ ID NO:307)		AA170-383;	PDZ domain 1-2 (of 2)		HVTILHKEEGAGLGFSLAGGADL	ENKVITVHRVFPNGLASQEGTIQ	KGNEVLSINGKSLKGTTHHDALA	ILRQAREPRQAVIVTRKLTPEAM	PDLNSSTDSAASASAASDVSVES	TAEATVCTVTLEKMSAGLGFSLE	GGKGSLHGDKPLTINRIFKGAAS	EQSETVQPGDEILQLGGTAMQGL	TRFEAWNIIKALPDGPVTIVIRR	KSLQSK <i>EFIVTD</i> (SEQ ID	NO:308)	
M68941							S81601														
protein- tyrosine	phosphatase	meg1					putative	interleukin	16	precursor											
PTN-4							prIL16														

IF 146HR		5′-	GTGGGATCCG   CTGGAATTCGC	AGATICAGGA   CTIGAAACTAC	GCAATGC-3' AAGTTC-3'	ID (SEQ ID	(56) NO:357)	0 N267-240	CIF 131KIR		1,0	AAAGGATCCA   TCACAATTGGA	CTACATCTTT   TAGCATATTGA	CCTCACG-3'   GGTCCAG-3'	(SEQ ID   (SEQ ID	358) NO:359)		N2290-2312   N2623-2595	3F 65RGR		5,'-	TGGGATCCCG   AGGAATTCCCA	CCCCCAAGGG ATTAATTTCAC	TGCGGAG-3'   TAC-3'	(SEQ ID (SEQ ID	360) NO:361)	_
/ 145HF		5′-	GTGG	AGAT	GCAA	(SEQ ID	NO:356)	N4-30	/ 130KIF		5'-	AAAG	CTAC	CCIC	(SEC	NO:358)		N229	/ 64RGF		5,-	TGGG	2222	TGCG	ČES)	NO:360)	
1	Eco RI		****						Bam HI	Eco RI	_	-							Bam HI	Eco RI							
AA4-85;	PDZ domain 1 (of 1)		RDSGAMLGLKVVGGKMTESGRLC	AFITKVKKGSLADTVGHLRPGDE	VLEWNGRLLQGATFEEVYNIILE	SKPEPQVELVVSRANSS (SEQ	ID NO:309)		AA766-870;	PDZ1 (of 1)		HYIFPHARIKITRDSKDHTVSGN	GLGIRIVGGKEIPGHSGEIGAYI	AKILPGGSAEQTGKLMEGMQVLE	WNGIPLTSKTYEEVQSIISQQSG	EAEICVRLDLNMLSNSS (SEQ	ID NO:310)		AA35-103;	PDZ domain 1 (of 1)		PPPRVRSVEVARGRAGYGFTLSG	QAPCVLSCVMRGSPADFVGLRAG	DQILAVNEINVKKASHEDVVKLI	GNSS (SEQ ID NO:311)		
AF007156							_		AB011131									-	AF035152								
	cal 41.8 kD	protein							KIAA0559			_			-		-		human	regulator	of G-	protein	signalling	12			
41.8 kD									K559										RGS12								

_										 
159KIR		- 2, -	AAAGGATCCC   TTAGAATTCTG	ATTTGGGAGAA	GGGTAAG-3'	(SEQ ID	NO:363)	N866-839		
158KIF		2, -	AAAGGATCCC	TCCGGCTCCT	CGGAAG-3'	(SEQ ID	NO:362)		N586-611	
Bam HI / 158KIF	Eco RI								-	
AB002314 AA197-284;	PDZ domain 1 (of 1)		PPAPRKVEMRRDPVLGFGFVAGS	EKPVVVRSVTPGGPSEGKLIPGD	QIVMINDEPVSAAPRERVIDLVR	SCKESILLTVIQPYPSPKRNSS	(SEQ ID NO:312)			
AB002314		-		_						
K316 KIAA0316									_	
K316										

1stPCR:	56DVISR		5′-	GCTCATGTCAC	TCTTCACCG-	3, (SEQ ID	NO:365)	N1195-1174		2 <sup>nd</sup> PCR,	nested:	38DVR		2,-	TCGGAATTCCC	AGCACTIGGCT	ACAG-3'	(SEQ ID	NO:367)		N1029-N1004	
1 <sup>st</sup> PCR:	55DVISF E		5′-	TCATCCAGAC	TCATCCGGAA	G-3,	(SEQ ID	NO:364) N	N652-673		2 <sup>nd</sup> PCR,	nested:	37DVF		5,-	TCGGATCCAA   1	ACGGTCACTC 7	TCAAC-3'	(SEQ ID	NO:366)	I	N723-747
Bam HI /	Eco RI																					
AA248-340;	PDZ domain 1 (of 1)		<b>QSTVLNIVTUNMERHHFLGIS</b>	IVGQSNDRGDGGIYIGSIMKGGA	VAADGRIEPGDMLLQVNDVNFEN	MSNDDAVRVLREIVSQTGPISLT	VAKCW <i>EFIVTD</i> (SEQ ID	NO:313)													0)0	
AF006011		,																				
human	dishevelled	segment	polarity	protein	homolog													•				
DVL1																						

137TR	5, -	ACGGAATTCCG	CTGGTTGGCGG	GCTTGAC-3'	(SEQ ID	NO:369)	N421-393		40TR		2,-	TCGGAATTCCT	CCAGCTCGGGG	T-3'	(SEQ ID	NO:371)	N3275-3253	
136TF	5′-	ACGGGATCCT	ACTGCCTGAG	ACCCACC-3'	(SEQ ID	NO:368)		N97-123	39TF		2,-	TCGGATCCAC	AGCATCCACA	TTGAG-3'	(SEQ ID	NO:370)	N2995-3019	
Bam HI /	ECO KI								/ IH meg	Eco RI								
AA35-137;	FDZ domain i (ol 1)	LLPETHRRVRLHKHGSDRPLGFY	IRDGMSVRVAPQGLERVPGIFIS	RLVRGGLAESTGLLAVSDEILEV	NGIEVAGKTLDQVTDMMVANSHN	LIVTVKPANQANSS (SEQ ID	NO:314)		AA1001-1088;	PDZ 1 (of 1)		HSIHIEKSDTAADTYGFSLSSVE	EDGIRRLYVNSVKETGLASKKGL	KAGDEILEINNRAADALNSSMLK	DFLSQPSLGLLVRTYPELE <i>EFIV</i>	<i>TD</i> (SEQ ID NO:315)		
AF028827		·							_MN	003253								
human tax	nreraction protein 40	4 ,							T- lymphoma	invasion	and	metastasis	inducing	protein 1				
TAX40									TIAM1									



protein  pDZ domains 1-2 (of 2)  SENCKDVFIEKQKGEILGVVIVE SGWGSILPTVIIANMHGGPAEK SGKLNIGDQIMSINGTSLVGLPL STCQSIIKGLENQSRVKLNIVRC PPVTTVLIRRPDLRYQLGFSVQN GIICSLMRGGIAERGGVRVGHRI IEINGQSVVATPHEKIVHILSNA VGEIHMKTMPAAMYRLLNSS (SEQ ID NO:316)	MINT1	human X11	L04953	AA717-894;	Eco RI /	34MIF	20MR
		protein		PDZ domains 1-2 (of 2)	Eco RI		
						5′-	2,-
				SENCKDVFIEKQKGEILGVVIVE		CGGAATTCGG	TCGGAATTCAG
				SGWGSILPTVIIANMMHGGPAEK		AAAACTGTAA	AAAACTGTAA CAGCCTGTACA
				SGKLNIGDQIMSINGTSLVGLPL		AGATG-3'	TCG-3'
				STCQSIIKGLENQSRVKLNIVRC		(SEQ ID	(SEQ ID
				PPVTTVLIRRPDLRYQLGFSVQN		NO:372)	NO:373)
SNA				GIICSLMRGGIAERGGVRVGHRI			
VGEIHMKTMPAAMYRLLNSS (SEQ ID NO:316)				IEINGQSVVATPHEKIVHILSNA		N2149-2167	N2690-2666
(SEQ ID NO:316)				VGEIHMKTMPAAMYRLLNSS			
				(SEQ ID NO:316)			

153KIR	5'- TGTGAATTCAA ATGGGGTAGTA GTGATTG-3' (SEQ ID NO:375)	N2237-2209
152KIF	5'- CTGGGATCCC ACATCAGCCG ATTGTGA-3' (SEQ ID NO:374)	N1948-1976 N2237-2209
Bam HI / 152KIF Eco RI		
Ab002301 AA652-742; PDZ domain 1 (of 1)	PHQPIVIHSSGKNYGFTIRAIRV YVGDSDIYTVHHIVWNVEEGSPA CQAGLKAGDLITHINGEPVHGLV HTEVIELLLKSGNKVSITTTPFE FIVTD (SEQ ID NO:317)	
Ab002301		
KIAA0303		
K303		

HI / 235CYF 236CYR RI	5'-	CCTGGATCCA TCAGAATTCCA	AAGAAAGCIT   TTAAGAGICTC	GTTACTGTG- TATC-3'	3' (SEQ ID	(SEQ ID NO:377)	NO:376) N535-510	
Bam HI Eco RI							-	
AF68836   AA85-176;   PDZ domain 1 (of 1)		QRKLVTVEKQDNETFGFEIQSYR	PONONACSSEMFTLICKIQEDSP	AHCAGLQAGDVLANINGVSTEGF	TYKQVVDLIRSSGNLLTIETLNG	NSS (SEQ ID NO:318)		
AF68836								
Cytohesin   binding	protein HE							
CBP								

189MR		2, -	CTCGAATTCCG	TGCTCAGGGCC	GCCCTA-3'	(SEQ ID	NO:379)	N165-138
188MF		5′-	ACTGGATCCC	CGTCACCACC	GCCATCATC-	3' (SEQ ID	NO:378)	N23-51
Bam HI /	Eco RI							
9110   AA11-52;	PDZ domain 1 (of 1)		PVTTAIIHRPHAREQLGFCVEDG	IVRPRPLAPGWGGRAALSTEFIV	TD (SEQ ID NO:319)			
AF029110								
IINT3 human MINT3 AF02			-					
MINT3								

198 TR	<del></del>	- 2	TGTGGAATTCC	TTGCGAGGCTC	CGTGAGC-3'	(SEQ ID	NO:381)	N429-401
/ 197 TF		- 2	AGGGGATCCG	CAAGGAGGTG	GAGGTGTTC-	3, (SEQ ID	NO:380)	=
Bam HI /	Eco RI							
8824 AA54-140;	PDZ domain 1 (of 1)		RKEVEVFKSEDALGLTITDNGAG	YAFIKRIKEGSVIDHIHLISVGD	MIEAINGQSLLGCRHYEVARLLK	ELPRGRTFTLKLTEPRK <i>EFIVTD</i>	(SEQ ID NO:320)	
AF028824								
human tax	interaction	protein 2						
TAX2								

A	4

					N154-182	
K561	KIAA0561	AB011133	133 AA948-1038;	/ IH me	161KIF	162KIR
			PDZ domain 1 (of 1)	Eco RI		
					5′-	2,-
			PPSLSTALARSTASACGRSASTW		CCTGGATCCC	GAGGAATTCTC
			VIATSTLCTTSSGVWRTEAPPRR		CCCATCGTTA	CAGGGCTGTGG
			RACGLGTSSPTSTGSQCWGWCTW		TCCACAGC-	TCCG-3'
			TSWSCCZRAATRYPCGPQPWR <i>IH</i>		3,	(SEQ ID
			RD (SEQ ID NO:321)		(SEQ ID	NO:383)
					NO:382)	
					N2836-2863 N3120-3095	N3120-3095

**PATENT** 

LU et al.

Application No.: 09/688,017

Page 4

A6

Please replace the paragraph (TABLE 4) beginning at page 60, line 1, with the following (see attached sheets).

Please replace the paragraph beginning at page 66, line 4, with the following:

--Other investigators have reported certain PL motifs important in PDZ binding, e.g., the C-terminal motifs S/T-X-V/I/L (for DLG1) and Y/F-Y/F-I/L/F for MPP1 (see, Doyle et al., 1996, Cell 85, 1067; Songyang et al., 1997, Science 275, 73). However, the reported motifs are not sufficiently specific (i.e. a large number of proteins meet these criteria yet are not necessarily actual PDZ ligands) and cover only a small number of PDZ proteins (approximately 10). The PRISM MATRIX can be used to determine ligand specificity and to deduce ligand binding motifs for any PDZ protein because it can precisely determine sequences of amino acids that do or do not result in specific PDZ binding. In addition, the assay has revealed a significant of new PDZ domain binding motifs (i.e. PL motifs): C-terminal sequence of CD6, ISAA (SEQ ID NO:14); C-terminal sequence of CD49E, TSDA (SEQ ID NO:24); C- terminal sequence of CD49F, TSDA (SEQ ID NO:24); C-terminal sequence of CLASP-1, SAEV (SEQ ID NO:289); C-terminal sequence of CLASP-4, YAEV (SEQ ID NO:228); C- terminal sequence of CD44, KIGV (SEQ ID NO:104); C-terminal sequence of IL5R, DSVF (SEQ ID NO:94); and C-terminal sequence of BLR-1, LTTF (SEQ ID NO:253). Identification of these novel PL sequences allows the definition of novel PL motifs (See TABLE 5A, infra). The specificity with which these novel motifs are defined is enhanced by the fact that the MATRIX reports both positive results (i.e. PDZ-PL) combinations that result in specific binding interactions) and negative results (i.e. PDZ-PL combinations that do not result in specific binding). For example, the Cterminal sequence of CD6, SAA and the C-terminal sequence of CD49E, SDA bind to the PDZ-domain polypeptide 41.8 while the related C-terminal sequence of CD166, TEA and Cterminal sequence of CD148, YIA do not. This identifies the novel PL motif (Motif 1, infra) of polypeptides terminating in alanine with serine at the -2 position and excludes polypeptides with threonine and tyrosine at the -2 position. This motif is therefore more specific than most previously identified motifs. Other novel motifs are described in TABLE 5A.--

Table 4	: PL Peptides						
CODE	PROTEIN NAME	GENBANK ACCESS	SEQUENCE	SEQ ID NO:			
AA1L	Clasp-1		ISKATPALPTVSISSSAEV	177			
AA2L	Clasp-2		ISGTPTSTMVHGMTSSSSVV	178			
AA3L	Clasp-4		CAISGTSSDRGYGSPRYAEV	179			
AA4L	CD3n	M33158	SVFSIPTLWSPWPPSSSSQL	180			
AA5L-M*	CD4	M12807	SEKKTSQSPHRFQKTCSPI	181			
AA6L	CD6	X60992	SPQPDSTDNDDYDDISAA	182			
AA7L	CD34	M81104	QATSRNGHSARQHVVADTEL	183			
AA9L	CD44	M69215	QFMTADETRNLQNVDMKIGV	184			
AA10L	CD46 (Form 1)	M58050	KKGTYLTDETHREVKFTSL	185			
AA11L	CD49E (4)	X06256	PYGTAMEKAQLKPPATSDA	186			
AA12L	CD49F	X53586	HKAEIHAQPSDKERLTSDA	187			
AA13L	CD95	M67454	KDITSDSENSNFRNEIQSLV	188			
AA14L	CD97	X84700	TSGTGHNQTRALRASESGI	189			
AA15L	CD98	J02939	ERLKLEPHEGLLLRFPYAA	190			
AA16L	CD105	X72012	STNHSIGSTQSTPCSTSSMA	191			
AA17L	VCAM1	M73255	ARKANMKGSYSLVEAQKSKV	192			
AA18L	CD138	J05392	PKQANGGAYQKPTKQEEFYA	193			
AA19L	CD148	D37781	ENLAPVTTFGKTNGYIA	194			
AA20L	CD166	L38608	DLGNMEENKKLEENNHKTEA	195			
AA22L	DNAM-1	U56102	TREDIYVNYPTFSRRPKTRV	196			
AA23L-M*	FasL	U1:1821	SSKSKSSEESQTFFGLYKL	197			
AA25L	FceRIb	D10583	YSATYSELEDPGEMSPPIDL	198			
AA28L	CDW125 (IL5R)	X62156	EVICYIEKPGVETLEDSVF	199			
AA29.1L	CDW128A (IL8RA)	M68932	ARHRVTSYTSSSVNVSSNL	200			
AA29.2L	CDW128B (IL8RB)	M73969	KDSRPSFVGSSSGHTSTTL	201			
AA30L	LPAP	X81422	AWDDSARAAGGQGLHVTAL	202			
AA33L	KV1.3	AAC31761	TTNNNPNSAVNIKKIFTDV	203			
AA34.2L	NMDA	NP000824	LNSCSNRRVYKKMPSIESDV	204			
AA37L	Glycophorin C	AAA52574	QGDPALQDAGDSSRKEYFI	205			
AA38L	Neurexin	AB011150	SSAKSSNKNKKNKDKEYYV	206			
AA39L	Syndecan-2	A33880	GERKPSSAAYQKAPTKEFYA	207			
AA40L	DOCK2	BAA13200	LASKSAEEGKQIPDSLSTDL	208			
AA41L	CC CKR-1R	L09230	LERVSSTSPSTGEHELSAGF	209			
AA42L	CC CKR-2	U03882	GKGKSIGRAPEASLQDKEGA	210			
AA43L	. CC CKR-3	HSU28694	LERTSSVSPSTAEPELSIVF	211			
AA44L	CC CKR-4	X85740	DTPSSSYTQSTMDHDLHDAL	212			
AA45L	BLR-1	S56162	PSWRRSSLSESENATSLTTF	213			
AA47L	CD83	Z11697	VTSPNKHLGLVTPHKTELV	214			
AA48L	CD62E		SSSQSLESDGSYQKPSYIL	215			
AA49L	CD5	X04391	SMQPDNSSDSDYDLHGAQRL	216			
AA55L	CD148	D37781	TIYENLAPVTTFGKTIA	217			
*The Sequence studied is mutated at positions >10 amino acids from C-terminus to increase water solubility and/or							
	e intramolecular			I			

Application No.: 09/688,017

Page 5

Please replace the paragraph beginning at page 106, line 9, with the following:

--FIGURES 3A-H show the use of peptides to inhibit PL-PDZ interactions using the G assay described *supra*. In FIGURE 3A and B, the inhibiton assays were carried out using GST fusion proteins containing PDZ domains from DLG1 or PSD95 (see *supra* and TABLE 3). Binding of biotinylated PL peptides for CLASP-2, CD46, Fas, or KV1.3 (as listed in TABLE 4) was determined in the presence of various competitor peptides (at a concentration of 100 uM) or in the absence of a competitor (equalized as 100% binding). The competitor peptides were 8-mers peptides having the sequence of C-terminus of CLASP-2 (MTSSSSVV; SEQ ID NO:227), CD46 (REVKFTSL; SEQ ID NO:113), or Fas (TFFGLYKL; SEQ ID NO:83), a unlabeled

19-mer having the sequence of c-terminus of KV1.3 (i.e., non-biotinylated AA33L as listed in **TABLE 4**), or a peptide having the sequence of residues 64-76 of hemoglobin (Vidal et al., 1999, *J. Immunol.* 163, 4811), i.e., an unrelated competitor. The binding of biotinylated peptide (10 uM for Fas and KV1.3, 20 uM for CLASP-2 and CD46) to GST alone was subtracted from the binding to the fusion proteins to obtain the net signal for each experimental condition. This net signal was then normalized by dividing by the signal in the absence of competitor peptide and the data were plotted. Error bars indicated the standard deviation of duplicate measurements. Specific inhibition of CLASP-2 PL-DLG PDZ binding was observed with the CLASP-2 8-mer, the CD46

8-mer, the Fas 8-mer, and the KV1.3 peptide, but not in the absence of peptide or using an unrelated peptide.--

Please replace the paragraph beginning at page 106, line 26, with the following:

--FIGURES 3C-F show similar assays using shorter peptides to inhibit (e.g., a 3-mer and a 5-mer). FIGURES 3C-E show binding of biotinylated PL peptides for CLASP-2, CD46, Fas, or KV1.3, at the indicated concentration (as listed in TABLE 3) to GST fusion proteins containing PDZ domains from NeDLG, DLG1, or PSD95 in the absence or presence of 1 mM 3-mer peptide having the sequence of the C-terminus of Clasp 2 (SVV) (TABLE 3).

AX

LU et al. Application No.: 09/688,017

Page 6

FIGURE 3F shows the effect on binding of a 5-mer CD49E peptide (ATSDA; SEQ ID NO:25) to GST fusion proteins containing a PDZ domain from 41.8Kd.--

Please replace the paragraph beginning at page 109, line 3, with the following:

-- The C-terminal core sequence of CD49f is TSDA (SEQ ID NO:24). When naturally-occurring residues are added to the core sequence, LTSDA (SEQ ID NO:30), RLTSDA (SEQ ID NO:31), ERLTSDA (SEQ ID NO:32), and KERLTSDA (SEQ ID NO:33) AID may also be used to target a PDZ domain-containing protein in T cells .--

Please replace the paragraph beginning at page 109, line 11, with the following:

-- The C-terminal core sequence of CD83 is TELV (SEQ ID NO:248). When naturally-occurring residues are added to the core sequence, KTELV (SEQ ID NO:249), AII HKTELV (SEQ ID NO:250), PHKTELV (SEQ ID NO:251), and TPHKTELV (SEQ ID NO:252) may also be used to target a PDZ domain-containing protein in T cells.--

Please replace the paragraph beginning at page 110, line 21, with the following:

When naturally-occurring residues are added to the core sequence, SSAQV (SEQ ID NO:219), SSSAQV (SEQ ID NO:220), ISSSAQV (SEQ ID NO:221), and SISSSAQV (SEQ ID NO:222) may also be used to target a PDZ domain-containing protein in T cells.--

-- The C-terminal core sequence of CLASP-1 is SAQV (SEQ ID NO:218).

-- The C-terminal core sequence of CLASP-2 is SSVV (SEQ ID NO:223).

Please replace the paragraph beginning at page 110, line 25, with the following:

When naturally-occurring residues are added to the core sequence, SSSVV (SEQ ID NO:224), SSSSVV (SEQ ID NO:225), TSSSSVV (SEQ ID NO:226), and MTSSSSVV (SEQ ID NO:227) may also be used to target a PDZ domain-containing protein in T cells.--

A12

X13

: 49

LU *et al.*Application No.: 0

Application No.: 09/688,017

Page 7

Please replace the paragraph beginning at page 110, line 29, with the following:

--The C-terminal core sequence of CLASP-4 is YAEV (SEQ ID NO:228).

A14

When naturally-occurring residues are added to the core sequence, RYAEV (SEQ ID NO:229), PRYAEV (SEQ ID NO:230), SPRYAEV (SEQ ID NO:231), and GSPRYAEV (SEO ID NO:232) may also be used to target a PDZ domain-containing protein in T cells.--

Please replace the paragraph beginning at page 110, line 33, with the following:

K15

--The C-terminal core sequence of KV1.3 is FTDV (SEQ ID NO:238). When naturally-occurring residues are added to the core sequence, IFTDV (SEQ ID NO:239), KIFTDV (SEQ ID NO:240), KKIFTDV (SEQ ID NO:241), and IKKIFTDV (SEQ ID NO:242) may also be used to target a PDZ domain-containing protein in T cells.--

Please replace the paragraph beginning at page 111, line 3, with the following:

A16

When naturally-occurring residues are added to the core sequence, LSTDL (SEQ ID NO:244), SLSTDL (SEQ ID NO:245), DSLSTDL (SEQ ID NO:246), and PDSLSTDL (SEQ ID NO:247) may also be used to target a PDZ domain-containing protein in T cells.--

-- The C-terminal core sequence of DOCK2 is STDL (SEQ ID NO:243).

Please replace the paragraph beginning at page 111, line 22, with the following:

RIT

--The C-terminal core sequence of Syndecan-2 is EFYA (SEQ ID NO:89).

When naturally-occurring residues are added to the core sequence, KEFYA (SEQ ID NO:259), TKEFYA (SEQ ID NO:260), PTKEFYA (SEQ ID NO:261), and APTKEFYA (SEQ ID NO:262) may also be used to target a PDZ domain-containing protein in B cells.--

Please replace the paragraph beginning at page 111, line 26, with the following:

Application No.: 09/688,017

Page 8

AIS

--The C-terminal core sequence of BLR-1 is LTTF (SEQ ID NO:253). When naturally-occurring residues are added to the core sequence, SLTTF (SEQ ID NO:254), TSLTTF (SEQ ID NO:255), ATSLTTF (SEQ ID NO:256), and NATSLTTF (SEQ ID NO:257) may also be used to target a PDZ domain-containing protein in B cells.--

Please replace the paragraph beginning at page 114, line 5, with the following:

K19

--The C-terminal core sequence of CD105 is SSMA (SEQ ID NO:159). When naturally-occurring residues are added to the core sequence, TSSMA (SEQ ID NO:160), STSSMA (SEQ ID NO:161), CSTSSMA (SEQ ID NO:291) and PCSTSSMA (SEQ ID NO:162) may also be used to target a PDZ domain-containing protein in endothelial cells.--

Please replace the paragraph beginning at page 114, line 17, with the following:

A20

When naturally-occurring residues are added to the core sequence, QKSKV (SEQ ID NO:164), AQKSKV (SEQ ID NO:165), EAQKSKV (SEQ ID NO:166), and VEAQKSKV (SEQ ID NO:167) may also be used to target a PDZ domain-containing protein in endothelial cells.--

--The C-terminal core sequence of VCAM1 is KSKV (SEQ ID NO:163).

Please replace the paragraph beginning at page 114, line 23, with the following:

A2J

--FcεRIβ, CDw125, CDw128 and IL-8RB are transmembrane receptors expressed by mast cells, basophils and eosinophils. These receptors play a role in the activation of these cells to result in degranulation and histamine release in allergic reactions. The C-terminal core sequence of FcεRIβ is PIDL (SEQ ID NO:129). When naturally-occurring residues are added to the core sequence, PPIDL (SEQ ID NO:130), SPPIDL (SEQ ID NO:131), MSPPIDL (SEQ ID NO:132) and EMSPPIDL (SEQ ID NO:133) may also be used to target a PDZ domain-containing protein in mast cells. In addition, the residue E may be substituted with G to increase its binding affinity.--

LU et al. Application No.: 09/688,017

Page 9

Please replace the paragraph beginning at page 114, line 31, with the following:

A22

--The C-terminal core sequence of CDw125 is DSVF (SEQ ID NO:94). When naturally-occurring residues are added to the core sequence, EDSVF (SEQ ID NO:95), LEDSVF (SEQ ID NO:96), TLEDSVF (SEQ ID NO:97), and ETLEDSVF (SEQ ID NO:98) may also be used to target a PDZ domain-containing protein in mast cells.--

Please replace the paragraph beginning at page 115, line 1, with the following:

A23

--The C-terminal core sequence of CDw128 is SSNL (SEQ ID NO:69). When naturally-occurring residues are added to the core sequence, VSSNL (SEQ ID NO:70), NVSSNL (SEQ ID NO:71), VNVSSNL (SEQ ID NO:72), and SVNVSSNL (SEQ ID NO:73) may also be used to target a PDZ domain-containing protein in mast cells.--

Please replace the paragraph beginning at page 115, line 5, with the following:

A24

--The C-terminal core sequence of IL-8RB is STTL (SEQ ID NO:233). When naturally-occurring residues are added to the core sequence TSTTL (SEQ ID NO:234), HTSTTL (SEQ ID NO:235), GHTSTTL (SEQ ID NO:236) and SGHTSTTL (SEQ ID NO:237) may also be used to target a PDZ domain-containing protein in mast cells.--

Please replace the paragraph beginning at page 115, line 10, with the following:

A25

--The C-terminal core sequence of NMDA is ESDV (SEQ ID NO:263). When naturally-occurring residues are added to the core sequence, IESDV (SEQ ID NO:264), SIESDV (SEQ ID NO:265), PSIESDV (SEQ ID NO:266), and MPSIESDV (SEQ ID NO:267) may also be used to target a PDZ domain-containing protein in neuronal cells.--

Please replace the paragraph beginning at page 115, line 14, with the following:

Application No.: 09/688,017

Page 10

A28

-- The C-terminal core sequence of neurexin is EYYV (SEQ ID NO:268).

When naturally-occurring residues are added to the core sequence, KEYYV (SEQ ID NO:269), DKEYYV (SEQ ID NO:270), KDKEYYV (SEQ ID NO:271), and NKDKEYYV (SEQ ID NO:272) may also be used to target a PDZ domain-containing protein in neuronal cells.--

Please replace the paragraph beginning at page 115, line 19, with the following:

-- The C-terminal core sequence of Glycophorin C is EYFI (SEQ ID NO:273).

When naturally-occurring residues are added to the core sequence, KEYFI (SEQ ID NO:274), RKEYFI (SEQ ID NO:275), SRKEYFI (SEQ ID NO:276), and SSRKEYFI (SEQ ID NO:277) may also be used to target a PDZ domain-containing protein.--

Please replace the paragraph beginning at page 115, line 23, with the following:

--The C-terminal core sequence of CD148 is KTIA (SEQ ID NO:278). When naturally-occurring residues are added to the core sequence, GKTIA (SEQ ID NO:279), FGKTIA (SEQ ID NO:280), TFGKTIA (SEQ ID NO:281), and TTFGKTIA (SEQ ID NO:282) may also be used to target a PDZ domain-containing protein in epithelial or myeloid cells.--

Please replace the paragraph beginning at page 138, line 9, with the following:

--All peptides were chemically synthesized by standard procedures. The Tat-CD3 carboxyl terminus fusion peptide, (GYGRKKRRQRRRGPPSSSSGL, SEQ ID NO:174); Tat-CLASP1 carboxyl terminus fusion peptide, (GYGRKKRRQRRRGSISSSAEV, SEQ ID NO:175); Tat-CLASP2 carboxyl terminus fusion peptide, (GYGRKKRRQRRRGMTSSSSVV, SEQ ID NO:176); and Tat peptide, (GYGRKKRRQRRRG, SEQ ID NO:289); were dissolved at 1 mM in PBS, pH 7, or dH2O. Stock MBPAc1-16 peptide, (AcASQKRPSQRHGSKYLA; SEQ ID NO:290), was dissolved at 5 mM. All peptides were aliquoted and stored at -80°C until tested.--

Application No.: 09/688,017

Page 11

Please replace the paragraph beginning at page 140, line 24, with the following:

-- To detect such inhibition, it was necessary to synthesize an analogue of the CLASP2peptide AA2L that (1) retained similar DLG1 binding properties and (2) would not itself generate a signal in the assay selected to measure inhibition. Because most molecular interactions between PDZ proteins and their ligands involve only the C-terminal 6 amino acids of the ligand, an eight amino acid variant of the CLASP-2 peptide, MTSSSSVV (SEQ ID NO:227), was anticipated to retain similar DLG1 binding properties as the 20 amino acid AA2L CLASP-2 peptide. This eight amino acid CLASP-2 peptide (lacking a functional label) was therefore synthesized and purified by standard techniques as described supra. When 100 uM of the (functionally unlabeled) eight amino acid CLASP-2 peptide and 20 uM of the biotin-labeled AA2L CLASP-2 peptide were added simultaneously to DLG1 in a variant of the "G" assay (described supra), the binding of the labeled AA2L CLASP-2 peptide was, as predicted, inhibited by greater than 50% (FIGURE 3A). An analogous experiment in which the labeled AA2L CLASP-2 peptide was replaced with another labeled DLG1 ligand, labeled AAI3L Fas peptide demonstrated similar inhibition by the eight amino acid CLASP-2 peptide (FIGURE 3A). Thus, an effective inhibitor of DLG1-ligand binding (i.e. the eight amino acid CLASP-2 peptide MTSSSSVV; SEQ ID NO:227) with a known potency range (order of magnitude 21 uM) was designed based on knowledge of the affinity, 21 uM, with which a particular labeled ligand, the CLASP-2 peptide AA2L, bound to DLG1.--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 88, at the end of the application.

#### **REMARKS**

Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-383, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk.

